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Annual Flu Shots May Be of Little Benefit to the Elderly

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September 26, 2007 — The elderly may receive little to no benefit from annual influenza vaccinations, according to a review of current evidence study reported in the October issue of *Lancet Infectious Diseases*.

"Influenza vaccination policy in most high-income countries attempts to reduce the mortality burden of influenza by targeting people aged at least 65 years for vaccination," write Lone Simonsen, from George Washington University in Washington, DC, and colleagues. "However, the effectiveness of this strategy is under debate. Although placebo-controlled randomised trials show influenza vaccine is effective in younger adults, few trials have included elderly people, and especially those aged at least 70 years."

Nearly every year, winter influenza epidemics in the United States affect approximately 5% to 20% of the population, causing about 300,000 hospitalizations and 36,000 deaths. People aged 65 years and older account for up to 90% of all influenza-related deaths.

In most high-income countries, one of the strategies of vaccination policy against influenza is to target people 65 years of age and older in hopes of decreasing the mortality burden of influenza. However, the apparent benefits of this strategy may have been exaggerated by frailty selection bias, in which healthier elderly are vaccinated more often than frail elderly, as well as by the use of all-cause mortality and other nonspecific trial endpoints.

When these factors are considered, the authors suggest that the remaining evidence base is at present insufficient to determine the magnitude of the mortality benefit, if any, that influenza vaccination offers the elderly.

Few trials demonstrating the efficacy of influenza vaccination have included elderly people, but those that have done so have indicated that clinical benefits and antibody responses decrease as age increases for individuals older than 70 years.

In 1960, US policy began targeting influenza vaccination at individuals at high risk for poor outcomes by virtue of chronic comorbid conditions and/or advanced age. Other high-income countries have followed suit, and the World Health Organization has endorsed these policies. From 1980 to the present, vaccination coverage increased from 15% to 65%, but recent excess mortality studies have not documented a corresponding decrease in influenza-related mortality.

"Paradoxically, whereas those studies attribute about 5% of all winter deaths to influenza, many cohort studies report a 50% reduction in the total risk of death in winter — a benefit ten times greater than the estimated influenza mortality burden," the authors write. "New studies, however, have shown substantial unadjusted selection bias in previous cohort studies."

This review includes a suggested analytical approach to identify this type of residual bias, which should help elucidate what mortality benefits can and cannot reasonably be expected from influenza vaccination.

The authors recommend use of more specific endpoints in future trials. For example, vaccine effectiveness should be measured against laboratory-confirmed influenza virus. This highly specific outcome would yield more reliable estimates of vaccine efficacy, thereby justifying higher costs and labor involved in its measurement. In addition, use of actual virus surveillance data, and not the arbitrary 4-month period used at present, would help identify each seasonal epidemic period. Although performing randomized controlled trials may seem ethically problematic, the authors suggest that such

evidence is sorely needed.

Recognizing that the aged immune system may not efficiently respond to influenza vaccination should facilitate development of other options for influenza control, such as more immunogenic vaccines or larger doses of vaccine to be used in the elderly, a combination of live and killed vaccine formulations, more aggressive use of antivirals for treatment and prophylaxis, and indirect protection via increased vaccination of transmitter populations. Ongoing evaluation would need to determine the effectiveness of such approaches.

"While awaiting an improved evidence base for influenza vaccine mortality benefits in elderly people, we suggest that this group should continue to be vaccinated against influenza," the authors conclude. "Influenza causes many deaths each year, and even a partly effective vaccine would be better than no vaccine at all. But the evidence base concerning influenza vaccine benefits in elderly people does need to be strengthened."

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In an accompanying Comment, Tom Jefferson and Carlo Di Pietrantonj, from Cochrane Vaccines Field in Alessandria, Italy, discuss future options to resolve the present uncertainty regarding the efficacy of influenza vaccination in the elderly.

"Simonsen and colleagues suggest that refocusing on the likely complications of immune senescence would require vigorous pursuit of other options," Dr. Jefferson and Dr. Di Pietrantonj write. "They also confront the ultimate taboo that drew so much scorn in the evidence overview: doing randomised trials in elderly people to settle the issue conclusively. That suggestion, which seems to fly in the face of current policies, is in our opinion the only ethical and scientific way to have a definitive answer to the question of whether or not current influenza vaccines protect elderly people."

Dr. Jefferson has received consultancy fees from Sanofi Synthelabo and Roche. Dr. Di Pietrantonj reports no relevant financial relationships.

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